Amendments to the Claims

Please amend claims 1, 2, 20, 25, 31-37, 44, 49-50, 55-57, 59-60 and 76 as indicated in the listing of claims.

Please cancel claims 7, 17, 46-47 and 77 without prejudice or disclaimer.

Claims 5-6, 8-15, 26-27, 38, 43, 45, 53-54 and 62-75 were previously canceled without prejudice.

Claims 30 and 58 were previously withdrawn.

The listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A set of primers~~, comprising at least 8 primers~~ that selectively hybridize under highly stringent conditions to a nucleotide sequence flanking and within fifty nucleotides of each of polycystic kidney disease-associated protein-1 (PKD1) gene sequences set forth as:

nucleotides 2043 to 4290 of SEQ ID NO:1,
nucleotides 17907 to 22489 of SEQ ID NO:1,
nucleotides 22218 to 26363 of SEQ ID NO:1,
nucleotides 26246 to 30615 of SEQ ID NO:1,
nucleotides 30606 to 33957 of SEQ ID NO:1,
nucleotides 36819 to 37140 of SEQ ID NO:1
nucleotides 37329 to 41258 of SEQ ID NO:1, and
nucleotides 41508 to 47320 of SEQ ID NO:1,

or to a nucleotide sequence complementary thereto~~to the PKD1 gene sequences, wherein each primer of the set hybridizes to a nucleotide sequence flanking and within fifty nucleotides of any one of the PKD1 gene sequences~~,

wherein each of the primers ~~comprising~~ comprises a 5' region and adjacent 3' region,

the 5' region comprising a nucleotide sequence that selectively hybridizes to a PKD1 gene sequence as set forth in SEQ ID NO:1 and, optionally, to a ~~PKD1 gene~~ homolog sequence, wherein the 5' region comprises at least ten contiguous nucleotides, and

the 3' region comprising a nucleotide sequence that selectively hybridizes to a PKD1 gene sequence as set forth in SEQ ID NO:1, and not to a PKD1 gene homolog sequence, wherein the homolog sequence is a sequence having a high sequence identity to SEQ ID NO:1~~the PKD1 gene sequence~~,

provided the primer does not consist of a sequence as set forth in SEQ ID NO:11, SEQ ID NO:18, SEQ ID NO:52, or SEQ ID NO:60;

wherein the primers amplify at least a first and a second amplification product, and wherein two primers for the first amplification product are selected from the group consisting of SEQ ID NOs: 3, 4, 5 and 6, and two primers for the second amplification product are selected from the group consisting of SEQ ID NOs:19, 20, 21 and 22.

2. (Currently amended) The set of primers of claim 1,

wherein the 3' region comprises at least one 3' terminal nucleotide identical to a nucleotide that is 5' and adjacent to the nucleotide sequence of ~~the PKD1 gene~~ SEQ ID NO:1 to which the 5' region of the primer can hybridize, and

wherein said 3' terminal nucleotide is different from a nucleotide that is 5' and adjacent to a nucleotide sequence of the PKD1 homolog to which the 5' region of the primer can hybridize.

3. (Previously presented) The set of primers of claim 2, wherein the 3' region comprises 2 to 4 3' terminal nucleotides.

4. (Previously presented) The set of primers of claim 2, comprising a 5' region of 14 to 18 nucleotides and a 3' region of 2 to 6 nucleotides.

5.-6. (Canceled).

7. (Canceled).

8.-15. (Canceled).

16. (Previously presented) A solid matrix, comprising the set of primers of claim 1, wherein each of the primers is immobilized on the solid matrix.

17. (Canceled).

18. (Withdrawn) The solid matrix of claim 17, wherein the matrix comprises a plurality of primers, wherein said primers are degenerate with respect to one or more codons encoding a polypeptide having an amino acid sequence as set forth in SEQ ID NO:2.

19. (Original) The solid matrix of claim 16, wherein the solid matrix is a microchip.

20. (Currently amended) An isolated polynucleotide, comprising a contiguous sequence of at least ten nucleotides ~~substantially identical to a nucleotide sequence of SEQ ID NO:1 or to a nucleotide sequence complementary thereto, wherein the nucleotide sequence corresponds to~~ and is about 90% complementary to at least nucleotide ~~3336~~ 3335 and 3337 of a PKD1 polynucleotide as set forth in SEQ ID NO:1 ~~and wherein nucleotide 3336 is deleted~~.

21. (Original) A vector, comprising the polynucleotide of claim 20.

22. (Original) A host cell containing the vector of claim 20.

23. (Original) A solid matrix, comprising the polynucleotide of claim 20, wherein said polynucleotide is immobilized on the solid matrix.

24. (Original) The solid matrix of claim 23, wherein the polynucleotide comprises one of a plurality of polynucleotides, each of which is immobilized on the solid matrix.

25. (Currently amended) A method of detecting the presence or absence of a mutation in a PKD1 polynucleotide in a sample, the method comprising:

contacting nucleic acid molecules in a sample with a first set of primer pairs to amplify a first amplification product, wherein the set of primer pairs is selected from the group consisting of SEQ ID NOs: 3, 4, 5, and 6, ~~19, 20, 21 and 22, and~~ wherein the first set of primer pairs selectively hybridize under highly stringent conditions to a PKD1 polynucleotide comprising SEQ ID NO: 1 but not a PKD1 polynucleotide homolog; and

contacting the first amplification product with a second set of primer pairs to amplify a second amplification product, wherein the set of primer pairs is selected from the group consisting of SEQ ID NOs: 19, 20, 21 and 22, and wherein the second set of primer pairs selectively hybridize under highly stringent conditions to the first amplification product~~amplify a region of the PKD1 polynucleotide but not a PKD1 polynucleotide homolog, thereby generating a PKD1-specific amplification product under said conditions~~; and

identifying the presence or absence of a mutation in the ~~PKD1-specific~~ second amplification product, thereby detecting the presence or absence of a mutation in the PKD1 polynucleotide in the sample.

26.-27. (Canceled).

28. (Original) The method of claim 25, wherein amplification is performed by a polymerase chain reaction.

29. (Original) The method of claim 25, wherein the PKD1 polynucleotide is a variant PKD1 polynucleotide.

30. (Withdrawn) The method of claim 29, wherein the variant PKD1 polynucleotide comprises a nucleotide sequence substantially identical to SEQ ID NO:1, wherein nucleotide 474 is a T; nucleotide 487 is an A; nucleotide 4884 is an A; nucleotide 6058 is a T; nucleotide 6195 is n A; nucleotide 7376 is a C; nucleotide 7696 is a T; nucleotide 8021 is an A; nucleotide 9367 is a T; nucleotide 10143 is a G; nucleotide 10234 is a C; or nucleotide 10255 is a T.

31. (Currently amended) The method of claim 25, wherein identifying the presence or absence of a mutation in the second amplification product comprises determining the nucleotide sequence of the second amplification product.

32. (Currently amended) The method of claim 25, wherein identifying the presence or absence of a mutation in the second amplification product comprises determining the melting temperature of the second amplification product, and comparing the melting temperature to the melting temperature of a corresponding nucleotide sequence of SEQ ID NO:1.

33. (Currently amended) The method of claim 25, wherein identifying the presence or absence of a mutation in the second amplification product is performed using denaturing high performance liquid chromatography.

34. (Currently amended) The method of claim 25, wherein identifying the presence or absence of a mutation in the second amplification product is performed using matrix-assisted laser desorption time of flight mass spectrometry.

35. (Currently amended) The method of claim 25, wherein identifying the presence or absence of a mutation in the second amplification product is performed using high throughput conformation-sensitive gel electrophoresis.

36. (Currently amended) The method of claim 25, wherein identifying the presence or absence of a mutation in the second amplification product is performed by a method selected from single stranded conformation analysis, denaturing gradient gel electrophoresis, an RNAse protection assay, allele-specific oligonucleotide detection, an allele-specific polymerase chain reaction, and an oligonucleotide ligation assay.

37. (Currently amended) The method of claim 25, wherein identifying the presence or absence of a mutation in the second amplification product is performed using a primer extension reaction assay,

wherein the primer extension reaction is performed using a detectably labeled primer and a mixture of deoxynucleotides and dideoxynucleotides, and

wherein the primer and mixture are selected so as to enable differential extension of the primer in the presence of a wild type PKD1 polynucleotide as compared to a mutant PKD1 polynucleotide.

38. (Canceled).

39. (Original) The method of claim 25, wherein the method is performed in a high throughput format using a plurality of samples.

40. (Original) The method of claim 39, wherein plurality of samples are in an array.

41. (Original) The method of claim 40, wherein the array comprises a microtiter plate.

42. (Original) The method of claim 40, wherein the array is on a microchip.

43. (Canceled).

44. (Currently amended) A method of identifying a subject at risk for autosomal dominant polycystic kidney disease (ADPKD) ~~a PKD1-associated disorder~~, the method comprising:

contacting nucleic acid molecules in a sample from a subject with a set of primer pairs to amplify a first amplification product, wherein the sample is contacted with a first set of primer pairs selected from the group consisting of SEQ ID NOs: 3, 4, 5 and 6, and the ~~sample~~first amplification product is subsequently contacted with a second set of primer pairs to amplify a second amplification product, wherein the second set primer pairs is selected from the group consisting of SEQ ID NOs: 19, 20, 21 and 22, and wherein the primer pairs selectively hybridize to a PKD1 polynucleotide comprising SEQ ID NO: 1 and amplify a region of SEQ ID NO: 1 under conditions suitable for amplification of the PKD1 polynucleotide but not a PKD1 polynucleotide homolog by the primer pair, thereby generating a first and second amplification product; and

detecting the presence or absence of a mutation indicative of ADPKD ~~a PKD1-associated disorder~~ in the second amplification product,

wherein the absence of the mutation identifies the subject [[a]] is not at risk for ADPKD ~~a PKD1-associated disorder~~, and

wherein the presence of the mutation identifies the subject [[as]] is at risk for ADPKD ~~a PKD1-associated disorder~~.

45. (Canceled).

46.-47. (Canceled).

48. (Original) The method of claim 44, wherein the method is performed in a high throughput format.

49. (Currently amended) The method of claim 44, wherein detecting the presence or absence of a mutation indicative of ADPKD ~~a PKD1-associated disorder~~ in the amplification product comprises accumulating data representative of the presence or absence of the mutation.

50. (Currently amended) The method of claim 49, wherein the data is formatted into a report indicating whether a subject is at risk ~~of~~ for ADPKD ~~a PKD1-associated disorder~~.

51. (Original) The method of claim 50, further comprising transmitting the report to a user.

52. (Original) The method of claim 51, wherein transmitting the report comprises sending the report over the internet, by facsimile or by mail.

53.-54. (Canceled).

55. (Currently amended) The method of claim ~~53~~44, detecting the presence or absence of the mutation comprises determining the nucleotide sequence of the amplification product, and comparing the nucleotide sequence to a corresponding nucleotide sequence of SEQ ID NO:1.

56. (Currently amended) The method of claim ~~53~~44, wherein detecting the presence or absence of the mutation comprises determining the melting temperature of the amplification product, and comparing the melting temperature to the melting temperature of a corresponding nucleotide sequence of SEQ ID NO:1.

57. (Currently amended) The method of claim ~~53~~44, wherein detecting the presence or absence of the mutation is performed using denaturing high performance liquid chromatography.

58. (Withdrawn) The method of claim 44, wherein the mutation indicative of a PKD1 associated disorder comprises a nucleotide sequence substantially identical to SEQ ID NO:1, wherein nucleotide 3110 is a C; nucleotide 8298 is a G; nucleotide 9164 is a G; nucleotide 9213 is an A; nucleotide 9326 is a T; or nucleotide 10064 is an A.

59. (Currently amended). The method of claim 44, wherein the mutation indicative of ADPKD a ~~of PKD1 associated disorder~~ comprises a nucleotide sequence substantially identical to SEQ ID NO:1, wherein nucleotide 3336 is deleted.

60. (Currently amended). A method of diagnosing an autosomal dominant polycystic kidney disease (ADPKD) ~~a PKD1 associated disorder~~ in a subject, the method comprising:

amplifying a portion of a PKD1 gene but not a PKD1 gene homolog in a nucleic acid sample from a subject with a first set of primer pairs, wherein the first set of primer pairs is selected from the group consisting of SEQ ID NOs: 3, 4, 5 and 6 and wherein the primer pairs selectively hybridize to SEQ ID NO: 1 and amplify a region of SEQ ID NO: 1 to obtain a first amplification product;

amplifying the first amplification product with at least a second set of primer pairs to obtain a nested amplification product, wherein the second set of primer[[s]] pairs is selected from

the group consisting of SEQ ID NO:19, 20, 21 and 22, and wherein the second set of primer pairs is suitable for performing nested amplification of the first amplification product; and

determining whether the nested amplification product has a mutation associated with ADPKD ~~a PKD1-associated disorder~~,

wherein the presence of a mutation associated with ADPKD ~~a PKD1-associated disorder~~ is indicative of ADPKD ~~a PKD1-associated disorder~~, thereby diagnosing ADPKD ~~a PKD1-associated disorder~~ in the subject.

61. (Original) The method of claim 60, wherein the method is performed in a high throughput format using a plurality of nucleic acid samples.

62.-75. (Canceled).

76. (Currently amended) The method of claim 25 or 44, wherein prior to identifying the presence or absence of a mutation in the ~~PKD1-specific~~ second amplification product, the second amplification product is serially diluted to remove genomic contamination.

77. (Canceled).

78. (Previously presented) The method of claim 60, wherein prior to obtaining the nested amplification product, the first amplification product is serially diluted to remove genomic contamination.